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Case Report

Brain abscess secondary to medication-induced osteonecrosis of the jaw



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ABSTRACT

A 75-year-old woman was referred to our department because of delayed post-extraction healing of the tooth socket. Medical history included zoledronic acid administration from 2007 to 2013 for bone metastases of breast cancer. Therefore, she was diagnosed with medication-related osteonecrosis of the jaw (MRONJ). MRONJ is an adverse event often clinically encountered among patients undergoing chemotherapy. Initial treatment included local irrigation and antibiotic therapy, but as the symptoms continued to gradually worsen, curettage of the sequestrum was performed three times. Sequestration finally occurred in most of the maxilla. However, inflammation had spread from the masticator space through the foramen ovale, resulting in a brain abscess (left inferotemporal cortex). Surgical drainage was performed by the neurosurgeon, but the patient's symptoms failed to improve. She died on postoperative day 21. Brain abscess secondary to MRONJ is a rare condition and this is the first reported case resulting in patient death.

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1. Introduction

Bisphosphonates are commonly used as effective therapeutic drugs against metastatic cancer in bones, multiple myeloma, osteoporosis, and other diseases, but osteonecrosis has been a widely reported adverse event. We report a summary of our experience with a case of zoledronic acid-related osteonecrosis of the jaw (MRONJ) that followed an extremely poor course, with a brain abscess secondary to her MRONJ ultimately resulting in death.

2. Case

Patient: A 75-year-old woman.

First visit: January 2012.

Chief complaint: A socket that was not healing after tooth extraction.

History: After undergoing breast cancer surgery in 1998 (invasive ductal carcinoma, T1N0M0, Stage I), there was bone metastasis to the third lumbar vertebra as observed by MRI and bone scintigraphy in 2005. Therefore, she received radiotherapy (40 Gy) and hormone therapy. There was no radiation exposure to the jawbone. She was started on zoledronic acid in 2007 for bone metastasis of breast cancer, and thereafter, she had no change in bone metastasis. In 2013, she experienced rheumatoid arthritis symptoms, and was prescribed oral methotrexate (MTX) from January 2014 to June 2014.

2.1. History of present illness

Tooth extraction of maxillary left first molar was performed in May 2010 and tooth extraction of mandibular right second premolar was performed in August 2011 at a nearby dental clinic. Subsequently, she was referred to our hospital in January 2012 because the tooth sockets would not heal.

* AsianAOMS: Asian Association of Oral and Maxillofacial Surgeons; ASOMP: Asian Society of Oral and Maxillofacial Pathology; JSOP: Japanese Society of Oral Pathology; JSOMS: Japanese Society of Oral and Maxillofacial Surgeons; JSOM: Japanese Society of Oral Medicine; JAMI: Japanese Academy of Maxillofacial Implants.

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2.2. Treatment and course

At the first visit, an oral examination revealed bone exposure (more than 8 weeks longer) and purulent discharge at the corresponding sites in the mandibular right second premolar and corresponding sites in the maxillary left first molar portion. The tooth sockets in both the upper and lower jaws had failed to heal; there were no obvious signs of sequestration. Biopsy surgery on the six corresponding sites, conducted in February 2012, revealed pathologically diagnostic findings of sequestration and pyogenic granuloma (biopsy was repeated several times and there were no evidences of malignancy), resulting in a diagnosis of MRONJ stage 2 according to the clinical staging of the American Association of Oral and Maxillofacial Surgeons (AAOMS) [1,2]. The treatment strategy was continuous administration of zoledronic acid, with a strategy to regularly clean the locally affected area and administer antibiotics. Exacerbation of symptoms and pain were observed in maxillary left second premolar and maxillary left second molar in July 2012. After providing a full explanation of the possibility that aggressive surgical treatment could worsen symptoms, patient consent was obtained, and tooth extractions and sequestrectomy were performed. Her condition was stable for some time, but in April 2013, inflammation was found to have worsened, and sequestrectomy was performed on the corresponding site of the upper left molar region. Because her condition with regard to the bone metastasis of breast cancer had stabilized, administration of zoledronic acid was discontinued in May 2013 based on the judgment of her attending physician. In November 2013, her pain intensified significantly, and sequestrectomy was again performed on the upper left molar region to resolve the inflammation. Although we were unable to halt the progression of MRONJ and failed to produce an improvement in her symptoms, we were able to resolve her inflammation with antibiotic treatment during multiple hospitalizations. Gradually, the extent of sequestration expanded (Fig. 1), until nearly the entire left side of the maxilla had become sequestered, and sequestration had begun to progress as far as the left nasal cavity floor, infraorbital margin, and zygomatic arch (Fig. 2). In late December 2014, she complained of a fever of 39.5 °C and headache, and CT imaging showed that the inflammation had spread to the left temporal lobe area via the foramen ovale, continuously with the left



Fig. 1. Intraoral photograph. The extent of sequestration expanded until nearly the entire left side of the maxilla.

medial pterygoid muscle and left lateral pterygoid muscle periphery (masticatory space) (Fig. 3). It was decided that future treatment would require joint medical care with a neurosurgeon. Since our hospital does not have a neurosurgery department, she was transferred to a related hospital where she could receive joint medical care. Despite continued efforts to reduce inflammation with antibiotics, the ring-enhancing lesion characteristic of a brain abscess was observed in MRI (Fig. 4) performed on day 20 after transfer, and expansion of the abscess was evident. In late January 2015, with the consent of the patient and her family, the abscess was drained through an open craniotomy. Approximately 8 mL of purulent discharge was collected, but infecting bacteria were not identified. Despite abscess drainage via the open craniotomy, postoperative inflammation was difficult to control, and further expansion of the brain abscess and worsening of cerebral edema were observed; in late February, on day 21 after the drainage was performed, the patient died.

3. Discussion

Following a 2003 report on bisphosphonate-related osteonecrosis of the jaw (BRONJ) from the USA [3], multiple cases have been reported in Japan. Because osteonecrosis of the jaw can be caused

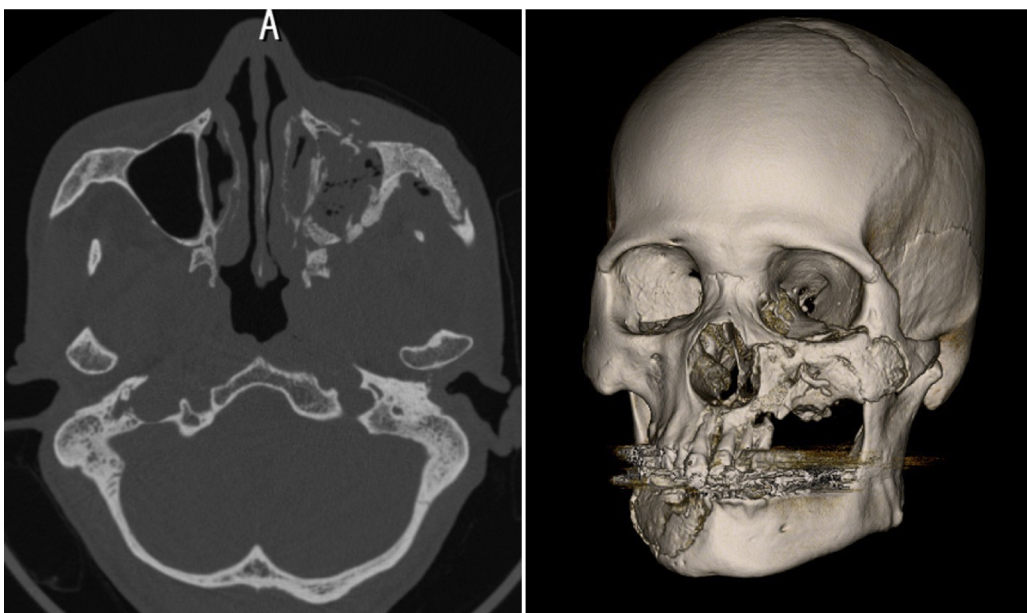


Fig. 2. CT and 3D reconstructed CT photography. CT shows sequestration over nearly the entire extent of the left half of the maxilla, reaching the infraorbital margin or zygomatic bone.

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